

U.S.S.N. 10/614,866

Filed: July 8, 2003

PRELIMINARY AMENDMENT

**In the Claims**

1. (original) An orally administerable abuse-deterrent pharmaceutical composition comprising a therapeutically effective amount of a drug prone to abuse selected from the group of compositions consisting of

(a) a composition comprising a therapeutically effective amount of a lipophilic derivative of a drug prone to abuse, and

(b) a water-insoluble, preferably lipophilic, formulation comprising a therapeutically effective amount of a drug prone to abuse.

2. (original) The composition of claim 1 comprising a therapeutically effective amount of a lipophilic derivative of a drug prone to abuse in one or more pharmaceutically acceptable excipients.

3. (original) The composition of Claim 1, wherein the composition is a controlled-release pharmaceutical composition.

4. (original) The composition of Claim 1, wherein the composition prevents the immediate release of a substantial portion of incorporated drug when the physical integrity of the composition is compromised and the resulting material is exposed to an aqueous medium.

5. (original) The composition of Claim 4, wherein the portion of the drug released immediately is less than 80% of the total amount of drug incorporated into formulation.

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6. (original) The composition of Claim 1, wherein the composition prevents the immediate release of a substantial portion of incorporated drug when the physical integrity of the composition is compromised and the resulting material is exposed to a non-aqueous medium.

7. (original) The composition of Claim 6, wherein the portion of the drug released immediately is less than 80% of the total amount of the drug incorporated into the composition.

8. (original) The composition of Claim 1 wherein the drug prone to abuse is selected from the group consisting of 1-phenylcyclohexylamine, 1-piperidinocyclohexanecarbonitrile, alfentanil, alphacetylmethadol, alphaprodine, alprazolam, amobarbital, amphetamine, anileridine, apomorphine, aprobarbital, barbital, barbituric acid derivative, bemidone, benzoylecgonine, benzphetamine, betacetylmethadol, betaprodine, bezitramide, bromazepam, buprenorphine, butabarbital, butalbital, butorphanol, camazepam, cathine, chloral, chlordiazepoxide, clobazam, clonazepam, clorazepate, clotiazepam, cloxazolam, cocaine, codeine, chlorphentermine, delorazepam, dexfenfluramine, dextromoramide, dextropropoxyphen, dezocine, diazepam, diethylpropion, difenoxin, dihydrocodeine, dihydromorphine, dioxaphentyl butyrate, dipanone, diphenoxylate, diprenorphine, ecgonine, enadoline, eptazocine, estazolam, ethoheptazine, ethyl loflazepate, ethylmorphine, etorphine, femproporex, fencamfamin, fenfluramine, fentanyl, fludiazepam, flunitrazepam, flurazepam, glutethimide, halazepam, haloxazolam, hexalgon, hydrocodone, hydromorphone, isomethadone, hydrocodone, ketamine, ketazolam, ketobemidone, levanone, levoalphacetylmethadol, levomethadone, levomethadyl acetate, levomethorphan, levorphanol, lofentanil, loperamide,

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loprazolam, lorazepam, lormetazepam, lysergic acid, lysergic acid amide, mazindol, medazepam, mefenorex, meperidine, meptazinol, metazocine, methadone, methamphetamine, methohexital, methotrimeprazine, methyldihydromorphinone, methylphenidate, methylphenobarbital, metopon, morphine, nabilone, nalbuphine, nalbupine, nalorphine, narceine, nefopam, nicomorphine, nimetazepam, nitrazepam, nordiazepam, normethadone, normorphine, oxazepam, oxazolam, oxycodone, oxymorphone, pentazocine, pentobarbital, phenadoxone, phenazocine, phencyclidine, phendimetrazine, phenmetrazine, pheneridine, piminodine, prodilidine, properidine, propoxyphene, racemethorphan, racemorphan, racemoramide, remifentanyl, secobarbital, sufentanyl, talbutal, thebaine, thiamylal, thiopental, tramadol, trimeperidine, vinbarbital, allobarbitone, alprazolam, amylobarbitone, aprobarbital, barbital, barbitone, benzphetamine, brallobarbital, bromazepam, brotizolam, buspirone, butalbital, butobarbitone, butorphanol, camazepam, captodiame, carbromal, carfentanyl, carpipramine, cathine, chloral, chloral betaine, chloral hydrate, chloralose, chlordiazepoxide, chlorhexadol, chlormethiazole edisylate, chlormezanone, cinolazepam, clobazam, potassium clorazepate, clotiazepam, cloxazolam, cyclobarbitone, delorazepam, dexfenfluramine, diazepam, diethylpropion, difebarbamate, difenoxin, enciprazine, estazolam, ethyl loflazepate, etizolam, febarbamate, fencamfamin, fenfluramine, fenproporex, fluanisone, fludiazepam, flunitraam, flunitrazepam, flurazepam, flutoprazepam, gepirone, glutethimide, halazepam, haloxazolam, hexobarbitone, ibomal, ipsapirone, ketazolam, loprazolam mesylate, lorazepam, lormetazepam, mazindol, mebutamate, medazepam, mefenorex, mephobarbital, meprobamate, metaclozepam,

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methaqualone, methohexital, methylpentynol, methylphenobarbital, midazolam, milazepam, morphine, nimetazepam, nitrazepam, nordiazepam, oxazepam, oxazolam, paraldehyde, pemoline, pentabarbital, pentazocine, pentobarbital, phencyclidine, phenobarbital, phendimetrazine, phenmetrazine, phenprobamate, phentermine, phenylacetone, pinazepam, pipradol, prazepam, proxibarbal, quazepam, quinalbaritone, secobarbital, secbutobarbital, sibutramine, temazepam, tetrazepam, triazolam, triclofos, zalepan, zaleplon, zolazepam, zolpidem, and zopiclone.

9. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is a free base or a free acid of the drug.

10. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is a salt comprising the ionized drug and a lipophilic counter-ion.

11. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is a complex comprising one or more components selected from the group consisting of drug molecules, metal cations, and lipophilic counter-ions.

12. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is a complex comprising one or more components selected from the group consisting of drug molecules, metal cations, and cyclodextrin molecules.

13. (original) The composition of Claim 2 wherein the drug is complexed with a metal cation selected from the group consisting of zinc, calcium, magnesium, bismuth and combinations thereof.

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14. (canceled)

15. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is a complex comprising the drug and a cyclodextrin.

16. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is an ester or amide formed between the drug and a fatty acid.

17. (original) The composition of Claim 1, wherein the drug is incorporated into a plurality of individual microparticles comprising a material that is either slowly soluble in water or water insoluble.

18. (original) The composition of Claim 17 wherein the microparticles comprise a wax or wax-like material.

19. (original) The composition of Claim 17 wherein the microparticles comprise a fat or a fatty substance.

20. (original) The composition of Claim 17 wherein the microparticles comprise a material selected from the group consisting of naturally water insoluble proteins, naturally water insoluble polysaccharides, naturally water insoluble lipids and phospholipids, cross-linked water soluble proteins, cross-linked water soluble polysaccharides, cross-linked water soluble cyclodextrins and combinations thereof.

21. (original) The composition of Claim 17 wherein the individual microparticles are coated with one or more independent layers, where at least one of the layers is water insoluble and is degraded by enzymes of the human gastrointestinal tract.

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22. (original) The composition of Claim 1 wherein the drug is in the form of individual drug particles coated with one or more independent layers where at least one of the layers is water insoluble and is degraded by enzymes of the human gastrointestinal tract.

23. (original) The composition of Claim 21 wherein at least one of the layers is water-insoluble, organic solvent-insoluble, and degradable by enzymes present in the human gastrointestinal tract.

24. (original) The composition of Claim 21 comprising materials wherein a combination of these materials is not soluble in water, organic solvent, or any combination thereof.

25. (original) The composition of Claim 21 wherein the composition is not completely soluble, and

wherein the drug is not fully released in a single solvent or enzyme solution.

26. (original) The composition of Claim 21 wherein the enzymatically degradable layer(s) comprise a material selected from the group consisting of naturally water insoluble proteins, naturally water insoluble polysaccharides, naturally water insoluble lipids and phospholipids, cross-linked proteins, cross-linked polysaccharides, and combinations thereof.

27. (original) The composition of Claim 1 wherein the drug prone to abuse is co-administered with a drug that has no appreciable abuse potential.

28. (original) The composition of claim 1 formulated for the drug to be immediately released upon oral administration.

29. (original) The composition of claim 1 wherein the drug prone to abuse is oxycodone.

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30. (original) A method of manufacturing an abuse-resistant pharmaceutical composition comprising homogeneously dispersing a therapeutically effective amount of a drug prone to abuse, in one or more pharmaceutically acceptable carrier(s), diluent(s), and/or additives, to form an orally administerable abuse-deterrent pharmaceutical composition comprising a therapeutically effective amount of a drug prone to abuse selected from the group of compositions consisting of

(a) a composition comprising a therapeutically effective amount of a lipophilic derivative of a drug prone to abuse, and

(b) a water-insoluble, preferably lipophilic, formulation comprising a therapeutically effective amount of a drug prone to abuse, as defined by any of claim 1.

31. (original) The method of claim 30 further comprising formulating the composition into a capsule or tablet.

32. (original) A method of administering an abuse-resistant pharmaceutical composition comprising orally administering to a patient in need thereof an abuse-deterrent pharmaceutical composition comprising a therapeutically effective amount of a drug prone to abuse selected from the group of compositions consisting of

(a) a composition comprising a therapeutically effective amount of a lipophilic derivative of a drug prone to abuse, and

(b) a water-insoluble, preferably lipophilic, formulation comprising a therapeutically effective amount of a drug prone to abuse, as defined by any of claim 1.